DETAILED OFFICE ACTION

Applicants response filed 03/02/2010 is acknowledged.

Claims 1-111, 119, 121, 122, 125, 126, 128-130, 135, 136, 140, 146, 154-160, 162-164, 169, 170, 174, 179, 191, 193-195, 198, 199, 201-203, 206-209, 213, and 218 are canceled. Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-226 are pending and currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180, and 181 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. It is noted that applicants amendments are sufficient to overcome the

basis of the previous rejection wherein the claims read on a computer program, per se. However, applicants amendments are not sufficient to overcome the remaining grounds of rejection, reiterated below. This rejection is maintained from the previous Office action.

Independent claim 149 has been amended to recite "A computer program product executed with a computer program". The recitation in the preamble of that the computer program is to be "executed with a computer" does provide any meaningful limitation on the instant claim. The invention is claimed as a computer program product, per se. Further compounding this issue is the limitations recited in the body of the instant claim comprising only process steps. The recited limitations in the body of the instant claim do not contain or involve any particular machine or apparatus ties. Further, the recited process steps are directed only to the intended functionality of manipulating data as suggested by the process steps recited in the body of the claimed computer program product. Therefore, the examiner can only conclude that the instant claims are directed to an unspecified computer program product, per se, and as such are still directed to non-statutory subject matter.

Response to Arguments

Applicant's arguments filed 03/02/2010 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 101 as being directed to non-statutory subject matter, applicants argue that amendments have been made to the instant claim to more clearly define what is being claims.

In response, applicants arguments are not persuasive because the amendments did not address the specific grounds maintained and discussed in the rejection above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and 221-226 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The Lancet*, 359:572-577 (February 16, 2002)) in view of Golub (*Science*, 286:531-537 (Oct.

15, 1999)). The rejection of claims 225 and 226 are necessitated by applicants amendments to the instant claims.

Petricoin discloses analyzing two biological state classes – "unaffected" and "affected" wherein the affected group is known to have cancer. Petricoin discloses analyzing two independent sets of samples. Specifically, one "sample" is composed of 50 control samples for preliminary analysis, other 17 control samples, and samples from cancer patients for preliminary analysis (*see* p. 572-573, Methods and *Study Population*; table 1; fig. 1, p. 575, and p. 576). Thus, the analysis of the original test data is analysis of "the first set" of samples. A second "sample set" is composed of 50 control samples for the masked analysis, other unaffected samples, and benign disease control samples (p. 573-573; fig. 1, p. 575, and p. 576). Petricoin teaches that results from the test (masked data) may be added to the model/dataset to improve prediction (p. 576, right col., third full paragraph). Therefore, Petricoin discloses that both "samples" were collected and separately statistically analyzed to classify samples into different biological states (*e.g.*, cancer and unaffected states) (fig. 1, p. 575, table 2, p. 576, left col.) AND also discloses an "intersection" subset (the totality of the data used for classification after "improvement"). Also, the results obtained from two independent samples (preliminary and masked) were "intersected" wherein data elements (key values for classifying samples, *e.g.*, M/Z) in the intersection subset is a member of both subsets (preliminary and masked samples) (p. 576). Petricoin teaches selecting a first subset of data elements from the first data (key M/Z values) (fig. 1 and p. 575 and 576). Petricoin further discloses a preanalytical variable, *e.g.*, medical status, a clinical

characteristic, medical condition (*e.g.*, premenopausal, menopause, age, benign diseases, *etc.*) and age distribution (*see* table 1, p. 573, p. 576). Petricoin discloses samples collected at different locations (*e.g.*, 100 control samples were provided from NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-573). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p. 575, left col.). Petricoin discloses reshuffling (resampling) of the two highest rated sets to form new subset candidates (p. 575). Petricoin discloses selecting candidate biomarker (CA125) and testing it on a validation data set (masked serum samples, p. 575 and p. 577). Petricoin discloses a biological state is a characteristic of presence of a disease (cancer) and a biomarker is a diagnostic of a disease (CA125). Petricoin teaches that values of data elements represent level of components (proteins, p. 572, right col.) in a data point sample (M/Z values determined by MS, p. 573; see also peaks on fig. 2). Expression of a law-molecular-weight protein (a cancer antigen CA125) is measured by coupling serum samples with a C16 hydrophobic interaction protein chip array (an immobilized capture affinity array) and the amount of the protein is measured by SELDI-TOF mass spectrometry (p. 573, right col.). The sample of Petricoin is serum and data collected from serum relate to the cellular localization of components in a sample (*e.g.*, components located in a soluble cell fraction or "attached" to suspended cell membranes) (p. 573, left col.). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p.

575, left col.). Petricoin also discloses "pattern-recognition" (p. 576, right col., third full paragraph, line 10). Petricoin discloses a "classification" as a pattern recognition process (fig. 1; p. 575, left col.).

Petricoin does not expressly teach selecting a second subset and displaying the intersection subset.

Golub discloses a method for classifying cancer by using gene expression monitoring (p. 531). Golub discloses using two classes (ALL and AML acute leukemia) and two samples comprising both classes (38 initial leukemia samples and independently collected 34 leukemia samples) (p. 532, 534). Golub discloses selecting "predictors" from the first sample (38 samples) and testing the predictors on an independent 34 leukemia samples (p. 532). Golub further discloses prediction strengths for both the initial (cross-validation) sample and an independent sample and selection of data elements with high prediction strength for both samples (selecting a first and a second subset) (p. 543 and fig. 3). Golub also discloses comparing two samples wherein the structure (data elements – gene predictors) in the initial sample is also seen in the independent sample (*i.e.*, samples are intersected) (p. 534, middle col. and fig. 4). Golub discloses displaying the intersection (fig. 3). Golub discloses that different types of samples, bone marrow and blood, were collected by different protocols (*e.g.*, samples from SJCRH were processed with a very different protocol) (p. 536-537, paragraph 23). Also, collection of bone marrow and blood requires different protocols. Golub discloses collecting samples at different collecting sites and from different populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to select both a first and a second subset of data elements and display the intersection, as taught by Golub, where the motivation would have been to test a model/hypothesis and to compare results from a model and a test, as taught by Golub, p. 534.

Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-226 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The Lancet*, 359:572-577 (February 16, 2002)) in view of Golub (*Science*, 286:531-537 (Oct. 15, 1999)), as applied to claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and 221-224 above, and in further view of Barnhill (U.S. Patent 6,789,069).

Petricoin and Golub make obvious claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 148, and 221-224, as set forth above.

Petricoin also discloses using mass spectrometry (*i.e.*, SELDI) for acquiring and processing experimental data and bioinformatics software for processing data (p. 573 and 575). Petricoin discloses a computer based chip system (the Protein Biology System 2 SELDI-TOF mass spectrometer such as Ciphergen Biosystems with a detector and a chip reader, p. 573). Petricoin also discloses that data were collected and were used later for analysis (*i.e.*, data are stored).

Petricoin and Golub do not disclose a supervised learning algorithm and specifically, a support vector machine analysis; protein binding partners in an expression profiling assay; and a computer system and a computer readable medium for performing the method.

Barnhill discloses a method for classifying unknown samples using a learning machine, similar to that of Petricoin. Barnhill discloses different methods for data acquisition such as nucleic acid arrays and protein expression assays (*e.g.*, antibody chips to identify specific proteins, col. 13, line 5-15). Barnhill method comprises acquiring expression data and processing data via creating training set by using a support vector machine and using the set to classify unknown data (col. 5, line 1-54). Barnhill discloses a gene chip, a mass spectrometer, and a protein binding assay comprising a protein binding partner (col, 1-2 and col. 13, line 5-15).

Barnhill discloses a computer system and a program for executing his method wherein data are entered into a computer system via a user interface (col. 22, line 27-67 and fig. 10-12), qualified, and selected (*see* for a general description of a computer system and programs col. 21, line 27 – col. 26, line 38 and fig. 10-12). The system comprises a processor, an input device, a memory, programs, and a network connector (fig. 10). Example 1 illustrates the method and the system for executing the method of Barnhill wherein tables 2-4 represent a database of ranked data obtained during the execution of the method (col. 38-42).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a supervised learning algorithm and

specifically, a support vector machine analysis, as taught by Barnhill, where the motivation would have been to improve pre-and post-processing data and maximize the value of genomic and proteomic information, as taught by Barnhill, col. 4, line 29-33. It would further have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a protein expression assay, as taught by Barnhill, where the motivation would have been to determine efficiently specific proteins from a large protein expression pool, as taught by Barnhill (col. 12, line 10 – col. 13, line 15). It would have also been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a computer and a computer readable medium for executing Petricoin's method, as taught by Barnhill, where the motivation would have been to manage large amount of complicated data in genomic and proteomic investigations, as taught by Barnhill, col. 1-2.

Response to Arguments

Applicant's arguments filed 07/16/2009 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and in further view of Barnhill,

Applicants argue that the claimed method requires the selection of first and second subsets of qualified common data elements from the first and second data sets, respectively, and further selecting an intersection subset of data elements from these

two subsets. Applicants argue that Nowhere does the Petricon reference teach or suggest the selection of subsets from the first and second data set. Applicants further argue that none of the Galub or Barnhill references cures the defects of the Petricon reference. Applicants further argue that none of the reference alone or in combination teaches or suggests the selection of first and second subsets of qualified common data elements from the first and second data sets, respectively, and further selecting an intersection subset of data elements from these two subsets as instantly claimed.

In response, the examiner maintains the position that applicants arguments are directed to the lack of a specific teaching or recitation of the exact data processing steps in the prior art as they appear and are recited in the instant claims. The examiner reiterates that the grounds of the instant rejection are based on obviousness following a consideration of the Graham v. Deere factors and, further, are not based on an assertion that the combination of the cited prior art provides an *ipsis verbis* recreation of the invention as recited in the instant claims.

The critical feature of the invention that applicants argue is sufficient to differentiate the instant claims over the prior art of record is the following limitation " the selection of first and second subsets of qualified common data elements from the first and second data sets, respectively, and further selecting an intersection subset of data elements from these two subsets".

In order to perform this, a practitioner must select a subset of data from a larger set of data. In order to meet the recitation of selecting a first subset from a first data set

and the selection of a second subset from a second data set, a practitioner must repeat, for a different set of data, the task of selecting a subset of data from a larger set of data. In order to meet the recitation of further "selecting and intersection of data elements from these two subsets", a practitioner must compare and contrast the contents of two data sets (generated by performing a data set and repeating on a different data set the task of selecting a subset of data from a large set of data) overlapping data (an intersection subset of data elements from these two subsets). Applicants argument can be reduced to an assertion that one skill in this art would not consider the act of generating two data subsets from two distinct, larger data sets and further compare and contrast the contents of the resultant subsets for overlapping data.

The examiner maintains that the teachings of the prior art render the above described data manipulation obvious with regard to the limitation argued by applicants; specifically "the selection of first and second subsets of qualified common data elements from the first and second data sets, respectively, and further selecting an intersection subset of data elements from these two subsets". The prior art of Petricon teaches the generation of two distinct data sets. In combination with Golub, the examiner maintains that it would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to select both a first and a second subset of data elements and display the intersection, as taught by Golub, where the motivation would have been to test a model/hypothesis and to compare results from a model and a test, as taught by Golub, p. 534. Such a combination would arrive the comparison and contrasting of two data subsets generated from two larger, but distinct,

sets of data and, further, result in their comparison and the selection of overlapping data content.

Applicants further argue that rejections on obviousness cannot be sustained by mere conclusory statements; instead there must be some rational underpinning to support the legal conclusions of obviousness. Applicants further cite KSR as support.

In response, the examiner notes that the instant rejection and the response to all arguments are based on the specific teachings of the prior art. Therefore the assertion that the rejection is based on mere conclusory statements is not persuasive.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ERIC S. DEJONG/
Primary Examiner, Art Unit 1631